Biodegradable polymers in tissue engineering and regenerative medicine

Properties, biocompatibility and applications

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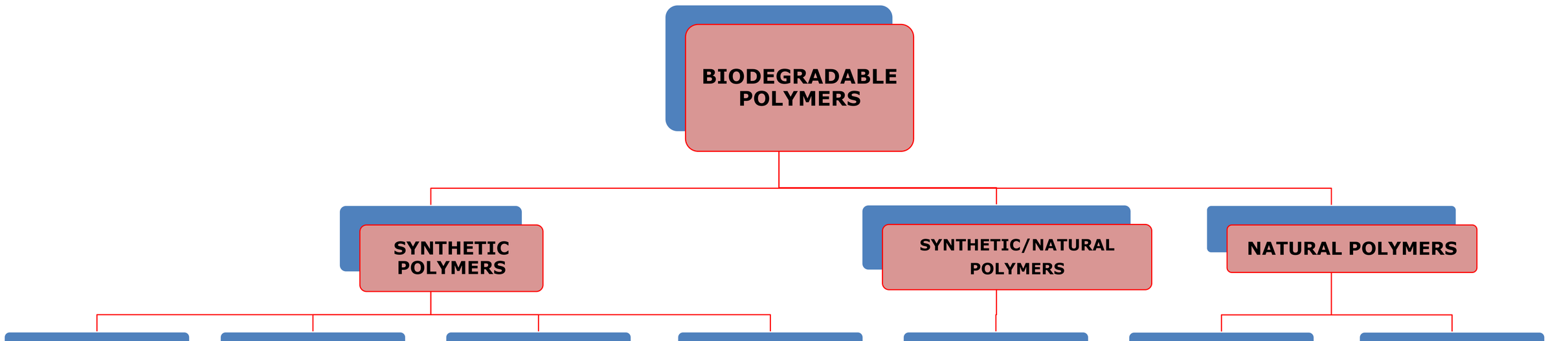
INTRODUCTION: WHAT IS TERM?

The "**TERM**" concept (Tissue Engineering and Regenerative Medicine) is the result of an evolution performed by the field of tissue engineering. It can be defined as a rapidly growing interdisciplinary field involving life, physical and engineering sciences and seeking to develop clinical therapies for the repair, maintenance, replacement and/or enhancement of biological function.

A very important role in TERM is played by biomaterials. A **biomaterial** is any natural or synthetic substance engineered to interact with biological systems in order to direct medical treatment. Depending on the target tissue to be engineered, the biomaterial that is used must exhibit several key characteristics, such as biocompatibility or biodegradability, and suitable mechanical properties. Thus, biomaterials are used for a large number of applications: bone and cartilage reconstruction, cardiovascular stents, soft tissue sutures, nerve reconstruction and drug delivery, among others.

BIODEGRADABLE POLYMERS

Polymers are long-chain molecules derived from repeating units, or monomers. Either natural or synthetic, polymers are one of the most researched biomaterials due to their suitable properties for many biomedical applications. **Biodegradability** is the property of being degradable in the presence of chemicals or enzymes in the body. The following hierarchical scheme classifies the biodegradable polymers analyzed in this review:



Properties:
- Hydrolytically degradable.
- It possesses chiral molecules.
- Long time to be resorbed.

Applications:
- Long-term scaffolds for bone, cartilage, tendon, neural and vascular regeneration.

Fig. 1: PLA scaffold for bone tissue regeneration.

Properties:
- Rapid degradation.
- Insolubility in common solvents.
- Hydrolytically degradable.

Applications:
- Short-term scaffolds for bone, cartilage, tendon, tooth, vaginal, intestinal, lymphatic and spinal regeneration.

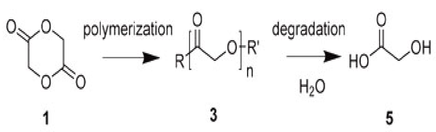


Fig. 2: Chemical structures of glycolide (1), the corresponding polymer PGA (3) and the degradation product: glycolic acid (5).

Properties:
- Different properties depending on the Lactic Acid-Glycolic Acid ratio.
- Hydrolytically degradable.

Applications:
- Drug delivery systems.
- Scaffolds for bone, cartilage, skin, tendon, liver and nerve tissue engineering.

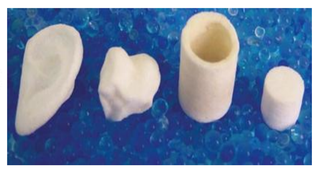


Fig. 3: Typical PLGA porous scaffolds with ear, joint, tube and cylinder shapes.

Properties:
- Different properties depending on side chain substitution (Figure 4).
- Hydrolytic degradability depending on the side chain substitution.

Applications:
- Drug delivery systems.

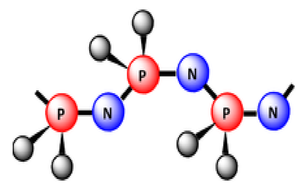


Fig. 4: Simplified general structure of a polyphosphazene molecule.

Properties:
- Long-time degradability.
- Intrinsic biocompatibility as it is found in cells of nearly all phyla.
- Hydrolytically degradable.

Applications:
- Long-term tissue engineering applications *e.g.* bone regeneration.

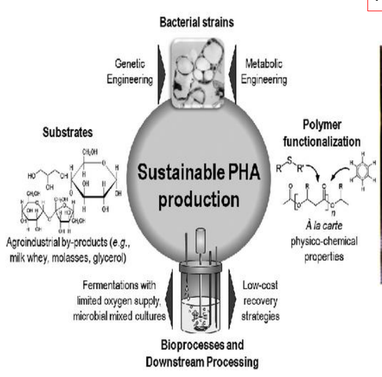


Fig. 5: Biotechnological production of PHA.

Properties:
- Hydrolytically stable.
- Mechanical strength.
- Enzymatically degradable.
- Intrinsic biocompatibility as it is the major protein in human body.

Applications:
- Scaffold for cartilage, tendon, ligament and skin regeneration.

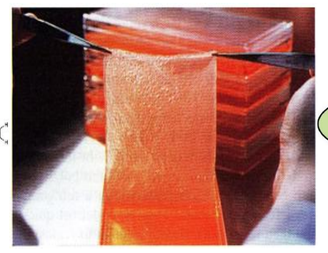


Fig. 6: Cultured dermal substitute composed of spongy collagen with fibroblasts.

Properties:
- Intrinsic biocompatibility as it is one of the main components of body tissues.
- Enzymatically degradable.

Applications:
- Hydrogels for cartilage, respiratory, vascular and nerve regeneration.

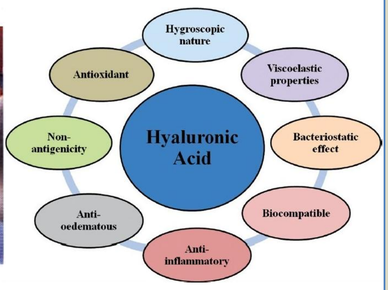


Fig. 7: Properties of hyaluronic acid.

BIOCOMPATIBILITY STUDIES

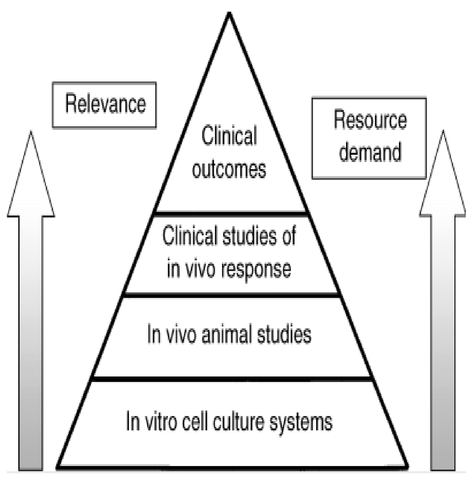


Fig. 8: Hierarchical representation of biocompatibility testing.

Before the approval of a biomaterial for medical use, it has to be proven that it is physically suitable and harmless to the body. The general process can be summarized into the next key points:

1) **Suitable physical properties:** depending on the proposed application different physical characteristics will be pursued and analyzed to determine the suitability of the analyzed material.

2) **In vitro cell culture systems**: cell viability, adhesion, proliferation and differentiation are analyzed in cell cultures. Genotoxicity and carcinogenicity tests are also often performed. Cytokine secretion of macrophages and other immunologic cells in front of the material and/or its possible degradation products (local effects) are also tested *in vitro.*

3) **In vivo animal studies**: inflammation capacity of the material can be observed *in vivo* in animal models (systemic effects). Immunogenic response of biomaterials is difficult to be studied as they can cause both short-term and long-term effects, as well as local or systemic inflammation.

4) **Clinical studies**: This is the final and more resource-demanding step before the approval of the biomaterial.

CONCLUSIONS

The field of Tissue Engineering and Regenerative Medicine is still new and therefore there is still a long way before this industry becomes one of the major ones, which is necessary if the total variety of patients are to be attended, but it has a promising potential. In fact, each year the number of publications is increasing as new materials, applications, properties or effects are achieved/observed.

The intergroup cooperation, the improvement of synthesis techniques, which can be either chemical or biotechnological depending on the biomaterial, and the advancements in biological research are leading to a better understanding of how biomaterials interact with hosts in cellular, tissue, organ and systemic levels.

RELEVANT REFERENCES

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